Received: 8 August 2017 | Revised: 8 September 2017 | Accepted: 16 September 2017

DOI: 10.1002/clc.22819

WILEY CLINICAL CARDIOLOGY

CLINICAL INVESTIGATIONS

Clinical outcomes according to symptom presentation in patients with acute myocardial infarction: Results from the FAST-MI 2010 registry

Etienne Puymirat[1] | Nadia Aissaoui[2] | Laurent Bonello[3] | Guillaume Cayla[4] | Jean-Noel Labèque[5] | Olivier Nallet[6] | Pascal Motreff[7] | Olivier Varenne[8] | François Schiele[9] | Jean Ferrières[10] | Tabassome Simon[11,12] | Nicolas Danchin[1] | for the FAST-MI Investigators

[1]Department of Cardiology, Assistance Publique-Hôpitaux de Paris (AP-HP), Hôpital Européen Georges Pompidou (HEGP), Paris, France; Université Paris-Descartes, Paris, France

[2]Intensive Care Unit, Assistance Publique-Hôpitaux de Paris (AP-HP), Hôpital Européen Georges Pompidou (HEGP), Paris, France

[3]Department of Cardiology, Assistance Publique-Hôpitaux de Marseille (AP-HM), Hôpital Nord, Marseille, France

[4]Department of Cardiology, University Hospital of Nimes, University of Nimes, France

[5]Department of Cardiology, Hôpital de Bayonne, Bayonne, France

[6]Department of Cardiology, Intercity Hospital Le Raincy-Montfermeil, Montfermeil, France

[7]Department of Cardiology, University Hospital of Clermont-Ferrand, UMR 6284 Auvergne University, Clermont-Ferrand, France

[8]Department of Cardiology, AP-HP, Hôpital Cochin, Université Paris-Descartes, Paris, France

[9]Department of Cardiology, University Hospital Jean Minjoz, Besançon, France

[10]Department of Cardiology, Rangueil Hospital, Toulouse, France

[11]Department of Clinical Pharmacology and Unité de Recherche Clinique (URCEST), AP-HP, Hôpital Saint Antoine, Paris, France

[12]Sorbonne Universités, UPMC Paris Univ-06, Paris, France

Correspondence
Etienne Puymirat, MD, PhD, Department of Cardiology, Hôpital Européen Georges Pompidou (HEGP), 20 Rue Leblanc, 75015 Paris, France
Email: etienne.puymirat@aphp.fr

Background: Atypical clinical presentation in acute myocardial infarction (AMI) patients is not uncommon; most studies suggest that it is associated with unfavorable prognosis.

Hypothesis: Long-term clinical impact differs according to predominant symptom presentation (typical chest pain, atypical chest pain, syncope, cardiac arrest, or dyspnea) in AMI patients.

Methods: FAST-MI 2010, a nationwide French registry, included 4169 patients with AMI in 213 centers at the end of 2010 (76% of active centers). Demographics, medical history, hospital management, and outcomes were compared according to predominant symptom presentation.

Results: Typical chest pain with no other symptom was reported in 3020 patients (68% in STEMI patients, 76% in NSTEMI patients). Atypical chest pain, dyspnea, syncope, and cardiac arrest were reported in 11%, 11%, 5%, and 1%, respectively. Patients with atypical clinical presentation had a higher cardiovascular risk profile and received fewer medications and a less invasive strategy. Using Cox multivariate analysis, atypical chest pain was not associated with higher death rate at 3 years (HR: 0.96, 95% CI: 0.69-1.33, $P = 0.78$), whereas cardiac arrest (HR: 2.44, 95% CI: 1.00-5.97, $P = 0.05$), syncope (HR: 1.70, 95% CI: 1.18-2.46, $P = 0.005$), and dyspnea (HR: 1.66, 95% CI: 1.31-2.10, $P < 0.001$) were associated with higher long-term mortality compared with patients with typical isolated chest pain. Similar trends were observed in STEMI and NSTEMI populations.

Conclusions: Atypical clinical presentation is observed in about 20% of AMI patients. Cardiac arrest, dyspnea, and syncope represent independent predictors of long-term mortality in STEMI and NSTEMI populations.

KEYWORDS

Acute Myocardial Infarction, Mortality, Symptom, Syncope

Funding information
FAST-MI 2010 is a registry of the French Society of Cardiology, supported by unrestricted grants from Merck, Eli Lilly, Daiichi Sankyo, AstraZeneca, Sanofi, GSK, and Novartis. None of the companies had a role in the design and conduct of the study or data collection and management. They were not involved in the analysis and interpretation of the data, nor in the preparation, review, or approval of this manuscript. The http://www.ClinicalTrials.gov identifier for FAST-MI 2010 is NCT01237418.

1 | INTRODUCTION

Atypical clinical presentation in acute myocardial infarction (AMI) patients is not uncommon. Registries show that up to 30% of AMI patients present with atypical symptoms, such as nausea/vomiting, shortness of breath, fatigue, palpitations, or syncope.[1] These symptoms are more often observed in the elderly, in females, and in patients with diabetes mellitus (DM), chronic renal disease, or dementia.[2–4] However, there is no precise definition of an atypical presentation that may also include cardiac arrest. Several studies have suggested that atypical complaints are associated with unfavorable prognosis.[1,5–8] These unfavorable outcomes may be partly attributable to a failure to use beneficial treatment strategies in these patients.

To our knowledge, no study has compared the prognostic impact of symptom presentation including syncope and cardiac arrest in AMI patients. Therefore, the aim of the present study was to assess the long-term prognostic impact according to predominant symptom presentation (typical isolated chest pain, atypical chest pain, syncope, cardiac arrest, or dyspnea) in AMI patients using data from the French Registry of Acute ST-elevation or non-ST-elevation Myocardial Infarction (FAST-MI) 2010 registry.

2 | METHODS

2.1 | The FAST-MI 2010 registry

FAST-MI 2010 is a national, prospective, multicenter registry including consecutive adult patients hospitalized for ST-segment elevation and non–ST-segment elevation AMI (with symptom onset ≤48 hours) over a period of 1 month (from October 2010). Patients with AMI following cardiovascular (CV) procedures were excluded. Participation in the study was offered to all intensive care units in French institutions (university teaching hospitals, general and regional hospitals, and private clinics) with the capacity to receive acute coronary syndrome emergencies. Details of the methodology have been described previously (see Supporting Information, eMethods 1, in the online version of this article).[9] The main objective of this registry was to evaluate practices for MI management in routine practice and to measure their association with outcomes over a 10-year follow-up.

The registry was conducted in compliance with Good Clinical Practice guidelines, French law, and the French data-protection law. The protocol was reviewed and approved by the Committee for the Protection of Human Subjects of Saint-Louis University Hospital, and the data file of FAST-MI was declared to the Commission Nationale Informatique et Liberté. The http://www.ClinicalTrials.gov identifier for FAST-MI 2010 is NCT01237418.

2.2 | Study population

A total of 4169 patients in 213 centers (76% of active centers in France) were included in this registry.[9] Baseline characteristics were collected prospectively. All data were recorded on computerized case-record forms by dedicated research technicians sent into each of the centers at least once a week. The research technicians also were asked to ensure that recruitment was consecutive. In the current analysis, we selected all AMI patients who underwent emergency coronary angiography for intended percutaneous coronary intervention (PCI). ST-segment elevation myocardial infarction (STEMI) was diagnosed when ST-segment elevation ≥1 mm was seen in ≥2 contiguous leads in any location on the index or qualifying electrocardiogram (ECG) or when presumed new Q waves were observed. Non–ST-segment elevation myocardial infarction (NSTEMI) was defined as the presence of elevated cardiac markers in the context of symptoms compatible with myocardial ischemia and no ST-segment elevation on the index or qualifying ECG.

Patients presenting with a suspected AMI were stratified according to whether their predominant presenting symptoms did or did not include typical isolated chest pain (ie, typical vs atypical presentation). We defined 4 classes of atypical presentation: atypical chest pain (including silent, nausea/vomiting, and fatigue), cardiac arrest, syncope, and dyspnea. High-grade atrioventricular block (HAVB) was defined as second-degree Mobitz II or third-degree atrioventricular block.

2.3 | Statistical analysis

For quantitative variables, means and SDs were calculated. In addition, medians with interquartile ranges were calculated when appropriate. Discrete variables are presented as number of events and percentages. Demographics, medical history, hospital management, and outcomes were compared according to these 5 groups for the present analysis. Comparisons were made with χ^2 or Fisher exact

tests for discrete variables, and by unpaired *t* tests, Mann–Whitney tests or 1-way ANOVA for continuous variables. Survival curves were estimated using the Kaplan–Meier estimators and compared using log-rank tests. Multivariate analyses of predictors of 30-day mortality were made using backward, stepwise multiple logistic regressions. Correlates of long-term survival were determined using a multivariate backward stepwise Cox analysis. Variables included in the final multivariate models were selected ad hoc, based upon their physiological relevance and potential to be associated with outcomes. Cumulative hazard functions were computed to assess proportionality. One model was used: adjusted on CV risk profile and management (medications and myocardial revascularization). Analyses were replicated using the same model in STEMI and NSTEMI.

For all analyses, a *P* value <0.05 was considered significant. Statistical analysis was performed using SPSS software version 23.0 (IBM Corp., Armonk, NY).

3 | RESULTS

3.1 | Patient characteristics according to initial presentation

Of the 4169 patients included in the registry, typical isolated chest pain was reported in 3020 patients (72% in all AMI patients; 68% in STEMI patients, 76% in NSTEMI patients). The rates of atypical chest pain (isolated), dyspnea, syncope, and cardiac arrest were 11%, 11%, 5%, and 1%, respectively. Typical chest pain was reported in 61% of patients with cardiac arrest, 64% of patients with syncope, and 63.5% of patients with dyspnea. Several CV risk profiles were observed according to initial presentation (Table 1). First, patients with atypical chest pain, dyspnea, and syncope were older compared with the patients with typical chest pain, whereas patients with cardiac arrest were younger. Early Global Registry of Acute Cardiac Events (GRACE) score was higher in all atypical presentations—140 ± 35 in patients with atypical chest pain, 156 ± 40 in patients with syncope, 175 ± 41 in patients with dyspnea, and 187 ± 41 in patients with cardiac arrest—compared with 134 ± 32 in patients with typical presentation. Finally, the proportion of STEMI was numerically higher in patients with syncope or cardiac arrest compared with patients with typical isolated chest pain.

For patient characteristics according to initial presentation in STEMI and NSTEMI patients, see Supporting Information, Tables 1 and 2 and Figures 1 and 2, in the online version of this article. Overall, the same trends were observed both in STEMI and NSTEMI populations.

3.2 | Initial management

Antithrombotic therapy differed strongly according to initial presentation (Table 2). Overall, all patients without typical isolated chest pain received less antiplatelet and anticoagulant therapy. Patients with cardiac arrest, however, received more glycoprotein IIb/IIIa inhibitors and patients with dyspnea received more anticoagulant medications. Recommended medications (eg, statins, β-blockers, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers) were less used in all groups of patients with atypical presentation. The use of coronary angiography and PCI was also lower in these patients, especially in those with atypical chest pain, dyspnea, or syncope. Finally, the rate of 2- or 3-vessel disease was higher in patients with dyspnea and those with syncope (see Supporting Information, Figure 3, in the online version of this article).

In STEMI patients, delay between symptom onset and first call was considerably greater in patients with atypical chest pain and dyspnea, whereas it was lower in patients with cardiac arrest or syncope. In addition, delay between ECG and primary PCI was higher in all groups of patients with atypical presentation, except in patients with syncope, in whom it was lower. The use of reperfusion therapies (eg, primary PCI or fibrinolysis) was similar to that in patients with typical isolated chest pain in all groups, except those with dyspnea, in whom it was significantly lower. Interestingly, the main culprit lesion in STEMI patients was the left anterior descending artery in patients with typical isolated chest pain (42%), cardiac arrest (49%), and dyspnea (36%); in patients with syncope, the main culprit lesion was the right coronary artery (58%), as in patients with atypical chest pain (40%; see Supporting Information, Figure 4, in the online version of this article). HAVB was observed preferentially in patients with syncope (18%). In NSTEMI patients, an invasive strategy was less frequently used in all patients without typical isolated chest pain.

3.3 | In-hospital complications and mortality at 30 days

In-hospital complications (recurrent MI, stent thrombosis, stroke, arrhythmia, and bleeding) were similar regardless of the initial clinical presentation. However, patients with cardiac arrest and syncope had more ventricular fibrillation, and patients with dyspnea had more ventricular tachycardia and stroke. The rate of major bleeding was higher in patients with syncope or dyspnea (Table 3). Finally, patients with atypical presentation received fewer recommended medications at discharge (see Supporting Information, Table 3, in the online version of this article).

At 30 days, the rate of death was higher in all groups of patients with atypical presentation compared with patients with typical isolated chest pain. Isolated atypical chest pain was associated with higher risk of 30-day death after adjustment (odds ratio [OR]: 3.06, 95% confidence interval [CI]: 1.81-5.17, $P < 0.001$), as was the case for patients with cardiac arrest (OR: 71.90, 95% CI: 32.03-161.39, $P < 0.001$), with syncope (OR: 3.82, 95% CI: 2.11-6.94, $P < 0.001$), or with dyspnea (OR: 2.27, 95% CI: 1.37-3.75, $P = 0.001$). Similar trends were observed in both STEMI and NSTEMI populations (data not shown).

3.4 | Long-term follow-up

The isolated atypical chest pain was not associated with higher rates of death at 3 years after adjustment on clinical presentation and in-hospital management (hazard ratio [HR]: 0.96, 95% CI: 0.69-1.33, $P = 0.78$), whereas cardiac arrest (HR: 2.44, 95% CI: 1.00-5.97,

TABLE 1 Baseline characteristics according to initial presentation

	Typical Chest Pain, n = 3020	Atypical Chest Pain, n = 442	Cardiac Arrest, n = 51	Syncope, n = 212	Dyspnea, n = 444	*P* Value
Age, y	63.1 ± 14.0	65.8 ± 14.8[a]	58.0 ± 13.4[b]	68.8 ± 13.7[a]	72.7 ± 12.4[a]	<0.001
Age > 75 y	768 (25)	154 (35)[a]	7 (14)	83 (39)[a]	234 (53)[a]	<0.001
Female sex	730 (24)	148 (33.5)[a]	17 (33)	74 (35)[a]	170 (38)[a]	<0.001
BMI, kg/m^2	26.9 ± 4.5	26.6 ± 4.6	26.4 ± 4.6	26.1 ± 4.3[b]	27.3 ± 5.1	0.03
Risk factors						
HTN	1494 (49.5)	244 (55)[b]	25 (49)	127 (60)[b]	336 (76)[a]	<0.001
DM	539 (18)	87 (20)	7 (14)	33 (16)	169 (38)[a]	<0.001
Current smoking	1138 (38)	143 (32)[b]	26 (51)	68 (32)	87 (20)[a]	<0.001
Dyslipidemia[c]	1306 (43)	199 (45)	15 (29)[b]	76 (36)[b]	210 (47)	0.02
CV history and comorbidities						
Previous MI	432 (14)	60 (14)	4 (8)	30 (14)	116 (26)[a]	<0.001
Previous PCI	446 (15)	61 (14)	4 (8)	21 (10)	90 (20)[b]	0.002
Previous CABG	173 (6)	26 (6)	2 (4)	15 (7)	32 (7)	0.67
Previous HF	64 (2)	13 (3)	1 (2)	12 (6)[b]	85 (19)[a]	<0.001
Previous stroke	123 (4)	25 (6)	1 (2)	8 (4)	39 (9)[a]	<0.001
PAD	186 (6)	43 (10)[b]	2 (4)	19 (9)	74 (17)[a]	<0.001
Chronic renal failure	94 (3)	15 (3)	0 (0)	9 (4)	56 (13)[a]	<0.001
Clinical presentation						
STEMI	1788 (59)	219 (49.5)[a]	37 (72.5)	133 (63)	187 (42)[a]	<0.001
GRACE score	134 ± 32	140 ± 35[b]	187 ± 41[a]	156 ± 40[a]	175 ± 41[a]	<0.001
LV function	53 ± 11	52 ± 11[b]	47 ± 15[b]	52 ± 13	45 ± 13[a]	<0.001
Prior medications						
Aspirin	613 (20)	106 (24)	7 (14)	41 (19)	143 (32)[a]	<0.001
Clopidogrel	331 (11)	55 (12)	3 (6)	23 (11)	103 (23)[a]	<0.001
β-Blockers	643 (21)	115 (26)[b]	11 (22)	50 (24)	170 (38)[a]	<0.001
Statins	815 (27)	115 (26)	14 (27.5)	45 (21)	162 (36.5)[a]	<0.001
ACEIs/ARBs	930 (31)	143 (32)	17 (33)	76 (36)	199 (45)[a]	<0.001

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CABG, coronary artery bypass grafting; CV, cardiovascular; DM, diabetes mellitus; GRACE, Global Registry of Acute Coronary Events; HF, heart failure; HTN, hypertension; LV, left ventricular; MI, myocardial infarction; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; SD, standard deviation; STEMI, ST-segment elevation myocardial infarction; TC, total cholesterol; TG, triglycerides. Data are presented as n (%) or mean ± SD.

[a] $P < 0.001$ (vs typical chest pain).

[b] $P < 0.05$ (vs typical chest pain).

[c] Included patients with previously documented diagnosis of hypercholesterolemia be treated with diet or medication or new diagnosis made during this hospitalization with elevated TC >160 mg/dL; did not include elevated TG.

P = 0.05), syncope (HR: 1.70, 95% CI: 1.18-2.46, *P* = 0.005), and dyspnea (HR: 1.66, 95% CI: 1.31-2.10, *P* < 0.001) were associated with higher long-term mortality compared with patients with typical isolated chest pain (Figure). Similar results were found after excluding patients who died within the first 24 hours. Finally, similar trends were also observed in both STEMI and NSTEMI populations (data not shown).

In patients with syncope as the predominant symptom, the rates of typical chest pain, left bundle branch block, right bundle branch block, any atrioventricular block, and ventricular fibrillation/tachycardia were 64%, 1.4%, 0.5%, 6%, and 4%, respectively. Using Cox multivariate analysis, syncope alone (ie, syncope accompanied with troponin rise without any typical chest pain, conduction, or rhythm disorder) was not also associated with higher 3-year death compared with patients with typical complaints (108 patients; HR: 1.24, 95% CI: 0.66-2.34, *P* = 0.50); however, syncope with typical chest pain without any conduction or rhythm disorder (64 patients; HR: 1.90, 95% CI: 1.06-3.40, *P* = 0.03) and syncope with conduction or rhythm disorders (40 patients; HR: 2.98, 95% CI: 1.62-5.48, *P* < 0.001) were associated with higher rates of death at 3 years.

4 | DISCUSSION

The present data from a nationwide registry indicate that about 20% of AMI patients presented with symptoms other than isolated typical chest pain. These patients (1) had a higher CV risk profile, whatever the predominant symptom (isolated atypical chest pain, syncope,

TABLE 2 In-hospital management according to initial presentation

	Typical Chest Pain, n = 3020	Atypical Chest Pain, n = 442	Cardiac Arrest, n = 51	Syncope, n = 212	Dyspnea, n = 444	*P* Value
Type of institution						
University hospital	1097 (36)	147 (33)[a]	20 (39)	64 (30)	168 (38)[a]	0.001
Community/Army hospital	1170 (39)	206 (47)	22 (43)	96 (45)	201 (45)	
Private clinic	753 (25)	89 (20)	9 (18)	52 (25)	75 (17)	
Medications in first 48 hours						
Aspirin	2950 (98)	419 (95)[b]	42 (82)[b]	201 (95)[a]	415 (93.5)[b]	<0.001
Clopidogrel	2407 (80)	352 (80)	33 (65)[a]	165 (78)	382 (86)[a]	0.001
Prasugrel	830 (27.5)	96 (22)[a]	10 (20)	50 (24)	53 (12)[b]	<0.001
GPIIb/IIIa	1167 (39)	147 (33)[a]	27 (53)[a]	66 (31)[a]	92 (21)[b]	<0.001
UFH	1284 (42.5)	162 (37)[a]	27 (53)	87 (41)	228 (51)[b]	<0.001
LMWH	1932 (64)	262 (59)	22 (43)[a]	126 (59)	221 (50)[b]	<0.001
Bivalirudine	110 (4)	7 (2)[a]	2 (4)	13 (6)	14 (3)	0.049
Fondaparinux	527 (17.5)	75 (17)	4 (8)	28 (13)	83 (19)	0.17
Statins	2739 (91)	371 (84)[b]	32 (63)[b]	180 (85)[a]	369 (83)[b]	<0.001
β-Blockers	2529 (84)	342 (77)[a]	22 (43)[b]	144 (68)[a]	314 (71)[b]	<0.001
ACEIs/ARBs	1379 (46)	175 (40)[a]	14 (27.5)[a]	79 (37)[a]	190 (43)	0.002
Procedures during hospitalization						
CAG during hospitalization	2934 (97)	403 (91)[b]	48 (94)	194 (91.5)[b]	362 (81.5)[b]	<0.001
PCI during hospitalization	2478 (82)	315 (71)[b]	42 (82)	159 (75)[a]	265 (60)[b]	<0.001
Radial access	2187 (75)	306 (76.5)	28 (58)[a]	123 (64)[a]	251 (70)	<0.001
DES	826 (33)	94 (30)	5 (12)[a]	45 (28)	89 (34)	0.02
Management in STEMI patients						
Symptoms to first call						<0.001
Median	75	90	39	30	120	
IQR	30–235	30–505	12–150	13.5–95.5	40–390	
ECG to primary PCI						<0.001
Median	108	131	119.5	98	138	
IQR	75.5–177.5	87–214	90.5–175.5	75–145	87–297	
Primary PCI	1132 (63)	143 (65)	25 (68)	86 (65)	95 (51)[a]	<0.001
Fibrinolysis	292 (16)	11 (5)[b]	5 (13.5)[a]	19 (14)	13 (7)[b]	<0.001
Management in NSTEMI patients						
CAG during hospitalization	1171 (95)	200 (90)[b]	12 (86)[a]	70 (89)[b]	199 (77)[b]	<0.001
PCI during hospitalization	862 (70)	135 (60.5)[b]	10 (71)	46 (58)[b]	132 (51)[b]	<0.001
PCI <24 h	279 (23)	32 (14)[b]	6 (43)[b]	12 (15)[b]	31 (12)[b]	<0.001

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CAG, coronary angiography; DES, drug-eluting stent; ECG, electrocardiogram; GPIIb/IIIa, glycoprotein IIb/IIIa; IQR, interquartile range; LMWH, low-molecular-weight heparin; NSTEMI, non–ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation; STEMI, ST-segment elevation myocardial infarction; UFH, unfractionated heparin. Data are presented as n (%) or mean ± SD.

[a] $P < 0.05$ (vs typical chest pain).

[b] $P < 0.001$ (vs typical chest pain).

cardiac arrest, or dyspnea); and (2) were less likely to receive invasive treatment and recommended medications. In addition, patients with cardiac arrest, dyspnea, or syncope concomitant with typical chest pain or conduction or rhythm disorders had higher long-term mortality after full adjustment on clinical presentation and management, compared with patients with isolated typical chest pain, both in STEMI and NSTEMI populations. In contrast, isolated atypical chest pain was not associated with higher long-term mortality.

In previous studies, atypical symptoms of AMI patients were usually defined as no chest pain or discomfort.[1,10,11] The incidence of atypical symptoms ranged from 8.4% in the GRACE study to 35.5% in the National Registry of Myocardial Infarction (NRMI) study.[1,10] In the present study, 18% of patients with AMI had an atypical presentation (ie, without typical isolated chest pain). Atypical presentations were associated with higher age, female sex, and more comorbid factors (including DM, hypertension, chronic kidney disease, and

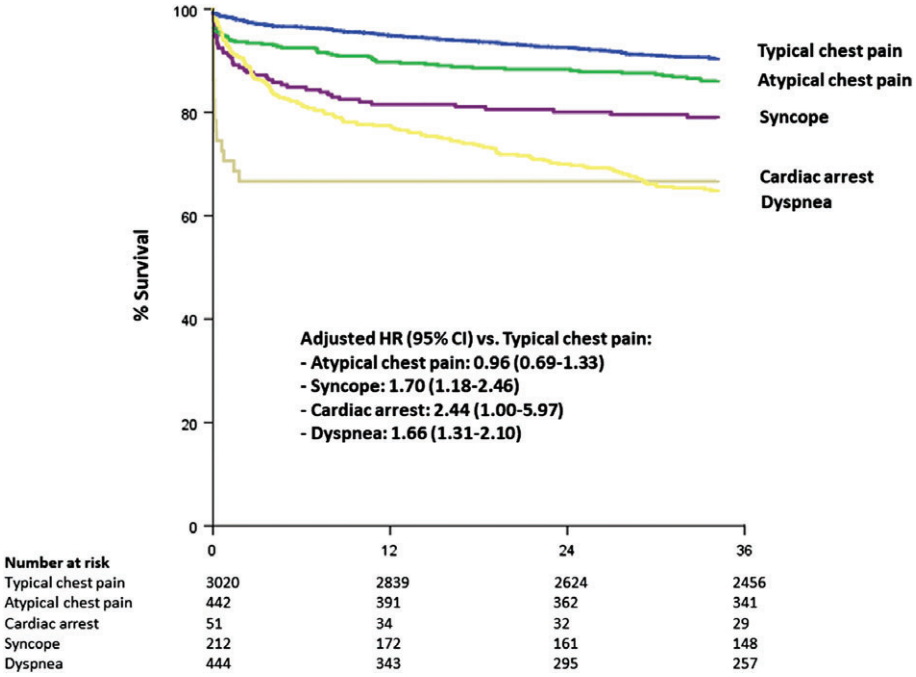

FIGURE 1 Three-year survival according to clinical presentation. Adjusted for age, sex, risk factors, comorbidities, type of MI, clinical presentation, medications used during the first 48 hours, and PCI. Abbreviations: CI, confidence interval; HR, hazard ratio; MI, myocardial infarction; PCI, percutaneous coronary intervention

TABLE 3 In-hospital complications and clinical outcomes according to initial presentation

	Typical Chest Pain, n = 3020	Atypical Chest Pain, n = 442	Cardiac Arrest, n = 51	Syncope, n = 212	Dyspnea, n = 444	*P* Value
Re-MI	32 (1)	5 (1)	0 (0)	1 (0.5)	6 (1)	0.80
Intrastent thrombosis	15 (0.5)	1 (0.2)	1 (2)	1 (0.5)	3 (0.7)	0.54
VF	49 (2)	7 (2)	11 (22)[a]	9 (4)[b]	6 (1)	<0.001
VT	75 (2.5)	12 (3)	2 (4)	9 (4)	22 (5)[b]	0.04
Stroke	7 (0.2)	2 (0.5)	0 (0)	0 (0)	6 (1)[a]	0.006
TIMI major	52 (2)	7 (2)	2 (4)	8 (4)[b]	19 (4)[a]	0.02
TIMI minor	79 (3)	9 (2)	3 (6)	7 (3)	14 (3)	0.48
Death at 30 d	46 (1.5)	24 (5)[a]	15 (29)[a]	18 (8.5)[a]	32 (7)[a]	<0.001
Death at 1 y	146 (5)	43 (10)[a]	17 (33)[a]	36 (17)[a]	98 (22)[a]	<0.001
Death at 3 y	281 (9)	60 (14)[a]	17 (33)[a]	44 (21)[a]	153 (34.5)[a]	<0.001

Abbreviations: Re-MI, recurrent myocardial infarction; SD, standard deviation; TIMI, Thrombolysis In Myocardial Infarction; VF, ventricular fibrillation; VT, ventricular tachycardia. Data are presented as n (%) or mean ± SD.

[a] $P < 0.001$ (vs typical chest pain).

[b] $P < 0.05$ (vs typical chest pain).

previous cardiovascular disease [except in patients with cardiac arrest]). These findings were consistent with those previously reported.[1,10]

Previous studies have suggested that atypical symptoms predicted adverse outcomes. In the NRMI study, in-hospital mortality was 20.0% in patients with atypical symptoms and 7.2% in those with typical symptoms.[10] The GRACE study also reported that atypical symptoms were associated with higher in-hospital mortality (13.0% vs 4.3%).[1] These unfavorable outcomes may be partly attributable to a higher delay in the recognition of diagnosis, which is particularly important for patients with STEMI, for whom early therapy is imperative; and they also may be attributable to a failure to use beneficial treatment strategies in both STEMI and NSTEMI patients. Recently, the Korea Acute Myocardial Infarction Registry (KAMIR) and the Japanese Registry of Acute Myocardial Infarction Diagnosed by Universal Definition (J-MINUET) studies reported that STEMI patients with atypical symptoms tended to be managed without primary PCI; and even if they were treated with urgent PCI, door-to-balloon time was longer.[7,11]

Cardiac arrest is well known to be an independent predictor of early and late mortality.[12] Similarly, patients with dyspnea as the predominant symptom had higher long-term mortality, likely explained by more frequent risk factors, previous cardiovascular disease (especially heart failure and comorbidities), and a greater burden of coronary artery disease. Patients with dyspnea represent 26% to 49% of acute coronary syndrome patients. Surprisingly, these patients are those who received the least invasive strategy and fewest recommended medications. In the GRACE study, patients with dyspnea also had higher in-hospital mortality (OR: 1.4, 95% CI: 1.1-1.9) as in the Gulf Registry of Acute Coronary Events (Gulf RACE) study.[1,8] Interestingly, patients with syncope are also associated with a worse clinical outcome. To our knowledge, few data are available related to syncope as presenting symptom in AMI patients. Patients with syncope were associated with higher in-hospital mortality in the GRACE

study (OR: 2.0, 95% CI: 1.4-2.9). The most frequently described explanation is a HAVB, which is reported between 3% and 13% in AMI patients and considered as a marker of worse outcomes.[13–16] Several independent predictors of HAVB have been previously described: older age, DM, Thrombolysis In Myocardial Infarction (TIMI) flow grade of 0/1 at presentation, the extent of myonecrosis, and an index right coronary artery lesion, which represents 58% in STEMI patients with syncope in our study.[17–22] Similarly, in the Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) trial, the right coronary artery index lesion was reported in 71% and was an independent predictor of HAVB (OR: 3.80, 95% CI: 1.94-7.45).[22] Finally, HAVB was described as an independent predictor of mortality at 1 year (adjusted HR: 2.45, 95% CI: 1.09-5.50) but not at 3 years.

Interestingly, our data show that in patients with syncope as the predominant symptom, compared with patients with isolated typical chest pain, the presence of typical chest pain (without any conduction or rhythm disorders) or the presence of conduction or rhythm disorders was associated with a higher mortality rate at 3 years, whereas there was no increased risk in patients presenting troponin-positive isolated syncope.

4.1 | Study limitations

Our study suffers the same limitations as all observational studies: namely, no causality can be asserted between parameters that are correlated. Comparisons between patients according to initial clinical presentation were not randomized and, despite careful adjustments on a large number of potentially confounding variables and the use of statistical adjustment with multiple methods yielding concordant results, our findings can only be considered indicative. The rate of silent ischemia was not recorded. Symptoms were analyzed as reported by the local investigators.

5 | CONCLUSION

Cardiac arrest, dyspnea, and syncope represent independent predictors of early and late mortality in both STEMI and NSTEMI populations, irrespective of the presence of typical chest pain. Isolated atypical chest pain was associated with higher early mortality but was not associated with long-term mortality. Finally, in patients with syncope as the predominant symptom, presence of concomitant typical chest pain and/or presence of conduction or rhythm disorders was associated with a higher long-term mortality, suggesting that syncope in patients with AMI should not be considered a benign symptom.

ACKNOWLEDGMENTS

The authors are deeply indebted to all patients who agreed to participate in the surveys and to the physicians who took care of the patients at the participating institutions.

Conflicts of interest

The authors declare no potential conflicts of interest.

ORCID

Etienne Puymirat http://orcid.org/0000-0002-0533-9682
Laurent Bonello http://orcid.org/0000-0002-3573-0244

REFERENCES

1. Brieger D, Eagle KA, Goodman SG, et al; GRACE Investigators. Acute coronary syndromes without chest pain, an underdiagnosed and undertreated high-risk group: insights from the Global Registry of Acute Coronary Events. *Chest*. 2004;126:461–469.
2. Canto JG, Fincher C, Kiefe CI, et al. Atypical presentations among Medicare beneficiaries with unstable angina pectoris. *Am J Cardiol*. 2002;90:248–253.
3. Mackay MH, Ratner PA, Johnson JL, et al. Gender differences in symptoms of myocardial ischaemia. *Eur Heart J*. 2011;32:3107–3114.
4. Rubini Gimenez M, Reiter M, Twerenbold R, et al. Sex-specific chest pain characteristics in the early diagnosis of acute myocardial infarction. *JAMA Intern Med*. 2014;174:241–249.
5. Uretsky BF, Farquhar DS, Berezin AF, et al. Symptomatic myocardial infarction without chest pain: prevalence and clinical course. *Am J Cardiol*. 1977;40:498–503.
6. Canto JG, Shlipak MG, Rogers WJ, et al. Prevalence, clinical characteristics, and mortality among patients with myocardial infarction presenting without chest pain. *JAMA*. 2000;283:3223–3229.
7. Fujino M, Ishihara M, Ogawa H, et al; J-MINUET Investigators. Impact of symptom presentation on in-hospital outcomes in patients with acute myocardial infarction. *J Cardiol*. 2017;70:29–34.
8. El-Menyar A, Zubaid M, Sulaiman K, et al; Gulf Registry of Acute Coronary Events (Gulf RACE) Investigators. Atypical presentation of acute coronary syndrome: a significant independent predictor of in-hospital mortality. *J Cardiol*. 2011;57:165–171.
9. Hanssen M, Cottin Y, Khalife K, et al; FAST-MI 2010 Investigators. French Registry on Acute ST-elevation and non ST-elevation Myocardial Infarction 2010. *Heart*. 2012;98:699–705.
10. Canto AJ, Kiefe CI, Goldberg RJ, et al. Differences in symptom presentation and hospital mortality according to type of acute myocardial infarction. *Am Heart J*. 2012;163:572–579.
11. Cho JY, Jeong MH, Ahn YK, et al; Korea Acute Myocardial Infarction Registry Investigators. Comparison of outcomes of patients with painless versus painful ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention. *Am J Cardiol*. 2012;109:337–343.
12. Priori SG, Blomström-Lundqvist C, Mazzanti A, et al. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: the Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). *Eur Heart J*. 2015;36:2793–2867.
13. Harpaz D, Behar S, Gottlieb S, et al. Complete atrioventricular block complicating acute myocardial infarction in the thrombolytic era. SPRINT Study group and the Israeli Thrombolytic Survey group. Secondary Prevention Reinfarction Israeli Nifedipine Trial. *J Am Coll Cardiol*. 1999;34:1721–1728.
14. Meine TJ, Al-Khatib SM, Alexander JH, et al. Incidence, predictors, and outcomes of high-degree atrioventricular block complicating acute myocardial infarction treated with thrombolytic therapy. *Am Heart J*. 2005;149:670–674.
15. Auffret V, Loirat A, Leurent G, et al. High-degree atrioventricular block complicating ST-segment elevation myocardial infarction in the contemporary era. *Heart*. 2016;102:40–49.
16. Kim HL, Kim SH, Seo JB, et al. Other Korea Acute Myocardial Infarction Registry, Korea Working Group on Myocardial Infarction Investigators. Influence of second- and third-degree heart block on 30-day

outcome following acute myocardial infarction in the drug-eluting stent era. *Am J Cardiol.* 2014;114:1658–1662.
17. Singh SM, FitzGerald G, Yan AT, et al. High-grade atrioventricular block in acute coronary syndromes: insights from the Global Registry of Acute Coronary Events. *Eur Heart J.* 2015;36:976–983.
18. Lee SN, Hwang YM, Kim GH, et al. Primary percutaneous coronary intervention ameliorates complete atrioventricular block complicating acute inferior myocardial infarction. *Clin Interv Aging.* 2014;9:2027–2031.
19. Nguyen HL, Lessard D, Spencer FA, et al. Thirty-year trends (1975–2005) in the magnitude and hospital death rates associated with complete heart block in patients with acute myocardial infarction: a population-based perspective. *Am Heart J.* 2008;156:227–233.
20. Birnbaum Y, Sclarovsky S, Herz I, et al. Admission clinical and electrocardiographic characteristics predicting in-hospital development of high-degree atrioventricular block in inferior wall acute myocardial infarction. *Am J Cardiol.* 1997;80:1134–1138.
21. Martin TN, Groenning BA, Murray HM, et al. ST-segment deviation analysis of the admission 12-lead electrocardiogram as an aid to early diagnosis of acute myocardial infarction with a cardiac magnetic resonance imaging gold standard. *J Am Coll Cardiol.* 2007;50:1021–1028.
22. Kosmidou I, Redfors B, Dordi R, et al. Incidence, predictors, and outcomes of high-grade atrioventricular block in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention (from the HORIZONS-AMI Trial). *Am J Cardiol.* 2017;119:1295–1301.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

How to cite this article: Puymirat E, Aissaoui N, Bonello L, et al. Clinical outcomes according to symptom presentation in patients with acute myocardial infarction: Results from the FAST-MI 2010 registry. *Clin Cardiol.* 2017;40:1256–1263. https://doi.org/10.1002/clc.22819